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September 15, 1992

Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Sir or Madam:

Subject: Report submitted in accordance with guidelines established by the U. S. Environmental Protection Agency Registration and Agreement for the TSCA 8(e) Compliance Audit Program

Report submitted by: Eastman Kodak Company
343 State Street
Rochester, NY 14650
(716) 724-4000
CAP Agreement Identification Number (8ECAP-0039)

The report pertains to N,N-dimethylaniline [CAS # 121-69-7] and is being submitted because of effects observed in a study conducted by multiple exposure routes. The title of the report being submitted is: "Basic Toxicity of N,N-Dimethylaniline". The latter report is being identified as a study involving other than human effects (Unit II.B.2.b of CAP Agreement).

Groups of five male rats were administered the test compound by gavage at 1000 or 100 mg/kg. There was a great decrease in feed intake and body weight gain in the high-dose group; all animals in this dose group died after two doses or were euthanatized due to poor condition. Hematologic changes in the single high-dose animal tested included a slight decrease in hemoglobin and hematocrit, increases in white blood count and polymorphonuclear leukocytes, and abnormal red blood cell morphology. Other abnormalities observed in the high-dose group included: increases in glutamic oxaloacetic transaminase, glucose, and urea nitrogen; large dark spleens, and brownish discoloration of blood and internal organs. Histopathologic changes in this group were bilateral tubular nephrosis, splenic congestion with lymphoid follicular hyperplasia, necrotic thymiditis, and hypertrophy of hepatic nuclei. Abnormal red blood cell morphology, enlarged dark spleens with splenic congestion, and gross increases in absolute and relative spleen weights were observed. A subsequent study at 10 mg/kg showed no compound-related effects.

This compound is used as an intermediate and sold as a pure chemical.

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3/2/95

Document Processing Center (TS-790) -- 2

Questions regarding this submission should be addressed to:

Mr. William Hart, Eastman Kodak Company
Corporate Health and Environment Laboratories
Rochester, NY 14652-3615
(716) 722-5991

Sincerely,

A handwritten signature in cursive script that reads "R. Hays Bell".

R. Hays Bell, Ph.D., Vice President
Corporate Health, Safety and Environment
(716) 722-5036

RHB:DRG
Enclosure

Basic Toxicity of N,N-Dimethylaniline

Toxicology Section

Written by: W. J. Krasavage

November 8, 1979

Basic Toxicity of N,N-Dimethylaniline

The approximate acute oral LD50 was 951 mg/kg for male rats and 1345 mg/kg for male mice. Weakness, rough coats, tremors, prostration, dark eyes and cyanosis were seen clinically. Application to the depilated abdomen of guinea pigs under an occlusive wrap for 24 hours produced slight skin irritation evidenced by slight to moderate edema and erythema within 24 hours and desquamation at one week. All animals were normal two weeks after treatment. The dermal LD50 is greater than 20 ml/kg. No evidence of percutaneous absorption was seen. Repeated applications (10) to the uncovered shaved backs of guinea pigs produced slight to moderate erythema after the initial dose, dry skin and scattered small eschars at one week and heavy eschars in 3/5 pigs at the end of treatment. The initial irritation produced was slightly exacerbated in 2/5 pigs and strongly exacerbated in 3/5 pigs by repeated applications. None of five guinea pigs tested for allergic skin reactions exhibited a positive response. A drop of the compound placed in the conjunctival sacs of six rabbit eyes (three unwashed and three washed) produced struggling, blinking and tightly closed eyes in all animals initially with slight erythema of the conjunctivae and nictitating membranes of all eyes and moderate edema on one unwashed eye at one hour after treatment. Twenty-four hours after treatment, all washed eyes were normal; all unwashed eyes showed slight to moderate erythema of the

conjunctivae and nictitating membranes and one eye had slight edema. The irides of two eyes were injected and the lower 1/2 of all corneas stained with fluorescein. The nictitating membrane of one eye stained with fluorescein. Forty-eight hours after treatment, one eye was normal, two had injected irides and slight erythema of the conjunctivae and nictitating membranes and one of these showed slight edema. At termination (14 days), two eyes were normal and the other showed slight erythema of the membrane. Irrigation with water immediately after treatment was definitely beneficial. The compound produced strong irritation in the unwashed eyes and was slightly irritating to the washed eyes.

Groups of five male rats were given 1000 and 100 mg/kg of the undiluted compound by gavage. A group of five control rats was given water. Two daily doses of 1000 mg/kg produced loss of coordination in the hindquarters, the animals were depressed within one hour of dosing, the eyes were dark, general appearance was poor and feet and skin were pale. Two rats died within eight hours after the second treatment and the other three were killed because of poor condition. These animals had a great reduction of feed intake and lost body weight. The mean absolute liver and kidney weights of the three euthanized animals appeared unaffected, but a slight increase in the relative weights of these organs reflected the loss of body weight. Only one of these animals was bled for hematologic and clinical chemistry determinations. Hemoglobin concentration, hematocrit and red blood cell count were slightly reduced. The total number of white blood cells and the absolute and relative

polymorphonuclear leukocytes were greatly increased. Morphology of the red cell was abnormal (polychromasia, anisocytosis, poikilocytosis and microcytosis). The serum levels of glutamic oxaloacetic transaminase were moderately increased and urea nitrogen and glucose were greatly increased.

Gross pathology at necropsy revealed pale skin and eyes, brownish color to blood and internal organs and large, dark spleens. Histopathologic changes seen in the 1000 mg/kg rats were bilateral tubular nephrosis (2/3), splenic congestion with lymphoid follicular hyperplasia (3/3), necrotic thymiditis (2/3) and hypertrophy of hepatic nuclei (1/3).

The 100 mg/kg animals received 11 doses over a 15 day period. Feed intake was normal and body weight gain was only slightly reduced compared to the controls. The absolute and relative spleen weights were greatly increased. The hemoglobin concentration, hematocrit and the total white blood cell and differential counts and the serum levels of glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, alkaline phosphatase, urea nitrogen and glucose were comparable to the controls. Lactic dehydrogenase was slightly increased and the red blood cell morphology was abnormal. Gross and histopathologic examinations revealed only splenic changes at this dose level. Grossly, the spleens were large and dark and histologically all spleens were congested and possibly hemorrhagic.

The sites of toxic action in the high dosed rats appeared to be the kidney, spleen, thymus, red blood cells and possibly the liver. In the low dosed animals, only the spleen and red blood cells were affected.

Because toxic effects were seen at both doses tested in this repeated gavage study, another study was done to establish a no-effect level. Groups of five male rats received 13 doses of 100, 10 or 0 mg/kg of the compound in 2.0% corn oil by gavage over a 17 day period. Feed intake, body weight gain, liver and kidney weights of both dose levels were normal. The abnormal red blood cell morphology, gross increase in spleen weights, the enlarged dark spleens seen grossly and the splenic congestion seen histologically in the 100 mg/kg dose rats of the initial study were reproduced by this dose level in the second study. In addition, the 100 mg/kg dose produced a slight increase in total white blood cells, absolute and relative polymorphonuclear leukocytes, mean corpuscular volume and mean corpuscular hemoglobin. The total red blood cell count, hematocrit and the hemoglobin concentrations were slightly decreased.

No compound related effects were seen in animals treated with 10 mg/kg of the compound. Thus, 13 doses of 10 mg/kg over a 17 day period was a no effect level.

WJK:bdo

SUMMARY OF BASIC TOXICITY

Chemical N,N-Dimethylaniline

Date 11-8-79

LD50 (mg/kg) P.O. Rats 951 (677-1336) Mice 1345 (957-1889)

Remarks: Weakness, rough coats, prostration, tremors, dark eyes, cyanosis

Guinea Pig Skin Irritation (covered) LD50 >20 ml/kg Absorption: ~~XXXXXX~~ evident

<u>Slight</u>	Moderate	Strong	Severe	<u>Not evident</u>
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Remarks:

Rabbit Eye Irritation

	Slight	Moderate	Strong	<u>Fluorescein stain</u>	
				Cornea	Adnexa
No. washed	3/3			0/3	0/3
No. unwashed		1/3	2/3	3/3	1/3

Remarks: Unwashed eyes showed moderate edema, injected irides, fluorescein staining of lower half of all corneas. Washed eyes showed only slight erythema of membranes. Irrigation was beneficial.

Skin Sensitization Potential No. guinea pigs 5

None 5/5	Weak	Moderate	Potent
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Remarks:

Repeated (10 days) Skin Application (uncovered) No. guinea pigs 5

Remarks: Slight to moderate erythema initially, dry skin and scattered small eschars at one week, heavy eschars (3/5 pigs) at end of treatment. Repeated doses produced slight exacerbation of initial response.

Acute Inhalation LC50 mg/m³ ppm Rats

Remarks: ND

Other tests:

SUMMARY OF BASIC TOXICITY--Repeat of Gavage Study

Repeated Exposure	Feeding	Drinking Water	<u>Gavage</u>	Inhalation
No. rats/group <u>5</u>	No. exposures <u>13</u>	No. days <u>17</u>	Carrier <u>none</u>	

Units of exposure:	%	<u>mg/kg</u>	mg/m ³	ppm
Exposure concentration:	<u>100</u>	<u>10</u>		<u>100</u>
				<u>10</u>

Weight gain	<u>N</u>	<u>N</u>	Hematology:	
Feed intake	<u>N</u>	<u>N</u>	Hgb.	<u>+1</u>
Daily dose (mg/kg/day)	<u>100</u>	<u>10</u>	Hct.	<u>+1</u>
Signs/behavior	<u>N</u>	<u>N</u>	WBC	<u>+1</u>
			Diff.	<u>Abn*</u>
			RBC	<u>+1</u>
			MCV	<u>+1</u>
			MCH	<u>+1</u>
			MCHC	<u>N</u>

*Slight increase in absolute and relative polymorphonuclear leukocytes, polychromasia, anisocytosis, poikilocytosis and Howell-Jolly bodies.

Clinical chemistry:

Organ weight:

GOT	<u>N</u>	<u>N</u>	Liver	
GPT	<u>N</u>	<u>N</u>	Abs.	<u>N</u>
LDH	<u>N</u>	<u>N</u>	Rel.	<u>N</u>
AP	<u>N</u>	<u>N</u>	Kidney	
UN	<u>N</u>	<u>N</u>	Abs.	<u>N</u>
Glucose	<u>N</u>	<u>N</u>	Rel.	<u>N</u>
SDH	<u>N</u>	<u>N</u>	Spleen	
			Abs.	<u>+3</u>
			Rel.	<u>+3</u>

Gross pathology: 100 mg/kg: Enlarged, dark spleens (2/5), whitish, fatty tissue on on peritoneum, pericardium and one lobe of lung (2/5).

10 mg/kg: Whitish fatty tissue same areas as above (1/5)

Histopathology: 100 mg/kg: Splenic congestion with lymphoid hyperplasia (4/5).
10 mg/kg: No compound related lesions. Whitish tissue seen grossly at both dose levels was lipoidal connective tissue.

Site of toxic action: 100 mg/kg: Red blood cell
10 mg/kg: No site of toxic action identified.

Legend

<u>↑</u>	Increased
<u>↓</u>	Decreased
<u>1</u>	Slight
<u>2</u>	Moderate
<u>3</u>	Great
<u>N</u>	Normal
<u>ND</u>	Not done



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

R. Hays Bell, Ph.D.
Vice President, Corporate Health, Safety, and Environment
Eastman Kodak Company
343 State Street
Rochester, New York 14650

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAY 08 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan
Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12652A



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contains at least 50% recycled fiber

Triage of 8(e) Submissions

Date sent to triage: MAY 01

NON-CAP

CAP

Submission number: 12652A

TSCA Inventory:

Y

N

D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO

AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX

SBTOX

SEN

W/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX

CTOX

EPI

RTOX

GTOX

STOX/ONCO

CTOX/ONCO

IMMUNO

CYTO

NEUR

Other (FATE, EXPO, MET, etc.):

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

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entire document: 0 1 2 pages 1, 2

pages 1, 2, DOBS

Notes:

Contractor reviewer: FOR

Date:

4/26/95

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: Submission # 8E1HQ-0992-12652 SEQ. # 1

TYPE: INT SUPP FLWP

SUBMITTER NAME: Festman Kodak Company

INFORMATION REQUESTED: FLWP DATE: 03/02/95

0501 NO INFO REQUESTED

0502 INFO REQUESTED (TECH)

0503 INFO REQUESTED (VOL ACTIONS)

0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:

0639 REFER TO CHEMICAL SCREENING

0678 CAP NOTICE

VOLUNTARY ACTIONS:

0401 NO ACTION REPORTED

0402 STUDIES PLANNED IN MAY

0403 NOTIFICATION OF WORK IN PROGRESS

0404 LABEL/MSDS CHANGES

0405 PROCESS/ANALYSIS CHANGES

0406 APP/USE DISCONTINUED

0407 PRODUCTION DISCONTINUED

0408 CONFIDENTIAL

SUB DATE: 09/15/92 OTS DATE: 09/24/92 CSRAD DATE: 03/02/95

CHEMICAL NAME: _____

CASE # 121-69-7

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEMPHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 ECOAQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCURRENCE/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQUEST DELAY	01 02 04	0248 PROD/USE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PRODCOMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	0259 OTHER	01 02 04
0211 CHR TOX (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0212 ACUTE TOX (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0229 METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0230 METAB/PHARMACO (HUMAN)	01 02 04		

USE: intermediate

TOXICOLOGICAL CONCERN:

SPECIES

ONGOING REVIEW

TRIAGE DATA: NON-CBI INVENTORY

LOW
MED
HIGH

RAT
MUS
GP
RGT

YES (DROP/REFER)
NO (CONTINUE)

YES
NO

CAS SR

LEFT-R

IN TANK

10/19/92

-CPSS- 0927952113

0 0 0 0 0 0 0 0 0 0 0

> <ID NUMBER>

8(E)-12652A

> <TOX CONCERN>

L/M

> <COMMENT>

ACUTE ORAL TOXICITY IN MALE RATS AND MALE MICE IS LOW CONCERN BASED ON LD50S OF 951 AND 1345 MG/KG, RESPECTIVELY. CLINICAL SIGNS INCLUDED WEAKNESS, ROUGH COAT, PROSTRATION, TREMORS, DARK EYES, AND CYANOSIS.

SKIN IRRITATION IN GUINEA PIGS IS LOW CONCERN. A 24 HOUR EXPOSURE PRODUCED SLIGHT SKIN IRRITATION EVIDENT BY MODERATE EDEMA, ERYTHEMA AND DESQUAMATION.

ACUTE DERMAL TOXICITY IN GUINEA PIGS IS LOW CONCERN WITH AN LD50 > 20 ML/KG. NO EVIDENCE OF PERCUTANEOUS ABSORPTION WAS NOTED.

REPEATED DERMAL IRRITATION IS MEDIUM CONCERN. 5 ANIMALS WERE ADMINISTERED 10 DOSES OF THE TEST MATERIAL. CLINICAL SIGNS INCLUDED SLIGHT TO MODERATE ERYTHEMA, DRY SKIN, SCATTERED SMALL ESCHAR, AND HEAVY ESCHAR. REPEATED DOSES PRODUCED SLIGHT EXACERBATION OF INITIAL RESPONSE.

SKIN SENSITIZATION IN GUINEA PIGS IS LOW CONCERN. NO POSITIVE REACTIONS WERE NOTED IN THE 5 ANIMALS TREATED.

EYE IRRITATION IN RABBITS IS MEDIUM CONCERN. A DROP OF TEST MATERIAL WAS ADMINISTERED IN 6 ANIMAL EYES (3 WASHED, 3 UNWASHED). CLINICAL OBSERVATIONS OF UNWASHED EYES INCLUDED MODERATE EDEMA, INJECTED IRIDES, FLUORESCIN STAINING OF LOWER HALF OF ALL CORNEAS. WASHED EYES EXHIBITED SLIGHT ERYTHEMA OF MEMBRANES.

SUBACUTE ORAL TOXICITY IN MALE RATS IS LOW CONCERN. GROUPS OF 5 ANIMALS WERE ADMINISTERED 100 OR 1000 MG/KG OF TEST MATERIAL. THE 100 MG/KG GROUP RECEIVED 11 DOSES OVER A 15 DAY PERIOD AND THE 1000 MG/KG GROUP RECEIVED 2 DAILY DOSES. THERE WAS NO MORTALITY AT 100 MG/KG LEVEL AND INCREASED ABSOLUTE AND RELATIVE SPLEEN WEIGHTS CHANGES AND HEMATOLOGIC CHANGES WERE NOTED. PATHOLOGY AND HISTOPATHOLOGY CHANGES IN THE 100 MG/KG GROUP INCLUDED ENLARGED, DARK SPLEEN AND SPLENIC CONGESTION, POSSIBLY HEMORRHAGIC. SITES OF TOXIC ACTION WERE THE SPLEEN AND RED BLOOD CELLS. IN THE 1000 MG/KG GROUP THERE WERE 2 MORTALITIES AND THE OTHER 3 WERE SACRIFICED DUE TO POOR HEALTH. CLINICAL OBSERVATIONS INCLUDED LOSS OF COORDINATION IN HINDQUARTERS, DEPRESSION, DARK EYES, AND PALE SKIN. INCREASE IN RELATIVE LIVER AND KIDNEY WEIGHTS AND HEMATOLOGY CHANGES WERE NOTED. PATHOLOGY AND HISTOPATHOLOGY CHANGES INCLUDED PALE EYES AND SKIN, BROWN BLOOD AND INTERNAL ORGANS, ENLARGED SPLEEN, BILATERAL TUBULAR NEPHROSIS, SPLENIC CONGESTION WITH LYMPHOID FOLLICULAR HYPERPLASIA, NECROTIC THYMITIS, AND HYPERTROPHIC HEPATIC NUCLEI. SITES OF TOXIC ACTION WERE KIDNEY, SPLEEN, THYMUS, RED BLOOD CELLS AND POSSIBLY LIVER. DUE TO THAT THE NOEL WAS NOT ESTABLISHED A SECOND STUDY WAS PERFORMED. GROUPS OF 5 MALE RATS RECEIVED 13 DOSES OF 10 OR 100 MG/KG OF TEST MATERIAL OVER 17 DAYS. HEMATOLOGY CHANGES AND AN INCREASE IN RELATIVE AND ABSOLUTE SPLEEN WEIGHT WERE ONLY NOTED AT THE 100 MG/KG LEVEL. PATHOLOGY AND HISTOPATHOLOGY CHANGES INCLUDED ENLARGED, DARK SPLEENS AND SPLENIC CONGESTION WITH LYMPHOID HYPERPLASIA (100 MG/KG), AND WHITISH, FATTY TISSUE ON PERITONEUM, PERICARDIUM AND ONE LOBE OF THE LUNG (10 AND 100 MG/KG). SITE OF TOXIC ACTION WAS NOTED AS THE RED BLOOD CELLS FOR 100 MG/KG AND NO SITE NOTED FOR 10 MG/KG.

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